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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/041,916	01/08/2002	Thomas W. Leonard	033218-016	4094

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EXAMINER

BADIO, BARBARA P

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 09/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	10/041,916	LEONARD, THOMAS W.
	Examiner Barbara P. Badio, Ph.D.	Art Unit 1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-19 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-19 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All
 - b) Some *
 - c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
 - a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>9,10</u> .	6) <input type="checkbox"/> Other: _____

Final Office Action

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

2. **The rejection of claims 2, 8, 14, 16 and 19 under 35 USC 112, first paragraph is withdrawn.**

Claim Rejections - 35 USC § 103

3. **The rejection of claims 1-19 under 35 USC 103(a) over Raijmakers et al. ('639), Simoons ('820), Raveendranath et al. ('717), Shah et al. ('039), Bender et al. ('638) and Kong et al. ('778) in combination is maintained.**

Applicant argues that none of the references teach or suggest the sulfatation of a mixture of "at least two alkali metal salts of estrogens". According to applicant, one may be encouraged to formulate a mixture of estrogenic sulfate esters but there is no motivation to make said mixture utilizing the claimed process. Applicant's argument was considered but not persuasive for the following reasons.

The issue is one of obviousness of the claimed process in the production of a known mixture. It is the examiner's position that the claimed process is *prima facie* obvious based on the combination of the above cited prior art and the level of skill of the ordinary artisan in the art at the time of the present invention.

Each of the recited steps of the claimed process is known in the art. Simoons ('820) teaches the production of a composition comprising a mixture of synthetic conjugated estrogens sulfate salt and Tris. Therefore, the production of a composition comprising a mixture of salts of synthetic estrogen sulfates and Tris is known in the art. Raijmakers et al. ('639) teach a method for the preparation of a mixture of alkali metal salts of estrogen sulfates by sulfatation of an estrogen mixture followed by conversion of said mixture of sulfates to the corresponding mixture of alkali metal salts of said estrogen sulfates. Kong et al. ('778) and Bender et al. ('638) teach a similar process for preparation of single alkali metal salts of estrogen sulfate. Unlike, Raijmakers et al., Kong and Bender, the claimed process recites sulfatation of the alkali metal salts of estrogens or production of the alkali metal salts of estrogens followed by sulfatation. However, (a) it has been held that merely reversing the order of steps in a multi-step process is not a patentable modification absent unexpected or unobvious results. Ex parte Rubin, 128 USPQ 440 (POBA 1959). Cohn v. Comr. Patents, 251 F.Supp. 437, 148 USPQ 486 (DC 1966) and (b) Shah ('039) and Raveendranath ('717) teach the production of alkali metal salts of estrogen sulfates by reaction of the alcohol with sodium hydride followed by sulfatation in the presence of a sulfur trioxide complex (see especially Example 1, '039; Examples 1-7, '717). Thus, the production of a mixture synthetic conjugated estrogens sulfate salt utilized in the composition of Simoons by reversal of the steps taught by Raijmakers et al. utilizing the process taught by Shah and Raveendranath would be *prima facie* obvious. It is also noted that Kong and Bender teach sulfatation in the presence of a sulfur trioxide complex. The motivation to

make the mixture is based on the knowledge in the art of the use of mixtures of conjugated estrogens, such as Premarin, in treatment of estrogen deficiency such as alleviation of the symptoms of menopausal syndrome. The motivation to utilize a mixture of alkali metal salts in the process taught by Shah and Raveendranath is based on (a) the knowledge in the art that individual alkali metal salts of estrogens can undergo sulfatation in the presence of a sulfur trioxide complex and, thus, the reasonable expectation that in combination each individual alkali metal salt would undergo sulfatation with the production of a mixture comprising sulfates of each alkali metal salts reacted and (b) the desire to obtain a one pot mixture of said alkali metal salts of estrogen sulfates for use as known in the art.

For these reasons and those given in Paper No. 5, the rejection of claims 1-19 under 35 USC 103(a) over Raijmakers et al. ('639), Simoons ('820), Raveendranath et al. ('717), Shah et al. ('039), Bender et al. ('638) and Kong et al. ('778) in combination is maintained.

Conclusion

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephone Inquiry

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio, Ph.D. whose telephone number is 703-308-4595. The examiner can normally be reached on M-F from 7:30am-4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308- 2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.


Barbara P. Badio, Ph.D.
Primary Examiner
Art Unit 1616

BB
September 23, 2003